

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

WHAT IS CLAIMED IS:

1. A composition comprising an antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
 - (b) a micelle-forming agent, and
 - (c) a biodegradable and biocompatible oil,
- said antigen formulation being formulated as a stable oil-in-water emulsion, said antigen formulation being substantially free of immunostimulating peptides and wherein said composition upon administration to an animal selected from the group consisting of humans, domesticated animals and agricultural animals is capable of inducing a specific cytotoxic T-lymphocyte response against the antigen contained in the composition.

2. The composition of claim 1, wherein said antigen is chosen from antigenic portions of the HIV antigens: gp160, gag, pol, Nef, Tat, and Rev; the malaria antigens: CS protein and Sporozoite surface protein 2; the Hepatitis B surface antigens: Pre-S1, Pre-S2, HBc Ag, and HBe Ag; the influenza antigens: HA, NP and NA; Hepatitis A surface antigens; Hepatitis C surface antigens, the Herpes virus antigens: EBV gp340, EBV gp85, HSV gB, HSV gD, HSV gH, HSV early protein product, cytomegalovirus gB, cytomegalovirus gH, and IE protein gp72; the respiratory syncytial virus antigens: F protein, G protein, and N protein; and the tumor antigens: carcinoma CEA, carcinoma mutated EGF receptor, prostate carcinoma specific antigen (PSA), prostate specific membrane associated antigen, carcinoma associated mucin, carcinoma P21, carcinoma P53, melanoma MPG, melanoma p97, MAGE-1, MAGE-3, gp100, MART-1, melanoma antigen gp75 carcinoma Neu oncogene product, carcinoma p53 gene product, and mutated p21 ras protein.

3. A composition comprising an antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion, said antigen formulation lacking immunostimulating peptides and wherein said composition upon administration to an animal selected from the group consisting of humans, domesticated animals and agricultural animals is capable of inducing a specific cytotoxic T-lymphocyte response against the antigen contained in the composition.

4. The composition of claim 3, wherein said antigen formulation consists essentially of said detergent, agent, and oil.

5. The composition of claim 3, wherein said antigen formulation is non-toxic to said human or domesticated or agricultural animal.

6. The composition of claim 3, wherein said antigen is chosen from the HIV antigens: gp160, gag, pol, Nef, Tat, and Rev; the malaria antigens: CS protein and Sporozoite surface protein 2; the Hepatitis B surface antigens: Pre-S1, Pre-S2, HBc Ag, and HBe Ag; the influenza antigens: HA, NP and NA; Hepatitis A surface antigens; Hepatitis C surface antigens; the Herpes virus antigens: EBV gp340, EBV gp85, HSV gB, HSV gD, HSV gH, HSV early protein product, cytomegalovirus gB, cytomegalovirus gH, and IE protein gp72; the respiratory syncytial virus antigens: F protein, G protein, and N - protein; and the tumor antigens: carcinoma CEA, carcinoma mutated EGF receptor, prostate

carcinoma specific antigen (PSA), prostate specific membrane associated antigen, carcinoma associated mucin, carcinoma P21, carcinoma P53, melanoma MPG, melanoma p97, MAGE-1, MAGE-3, gp100, MART-1, carcinoma Neu oncogene product, carcinoma p53 gene product, and mutated p21 ras protein.

7. A method for inducing a cytotoxic T-lymphocyte response in an animal selected from the group consisting of humans, domesticated animals and agricultural animals, comprising:

administering to said animal an admixture comprising an antigen and a microfluidized antigen formulation, said antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said admixture is administered to said animal in an amount sufficient to induce a cytotoxic T-lymphocyte response in said animal which is specific for the antigen contained in said admixture.

8. The method of claim 7, wherein said antigen formulation consists essentially of said detergent, agent, and oil.

9. The method of claim 7, wherein said method consists essentially of a single administration of said mixture to said human or said animal.

10. The method of claim 7, wherein said human or said animal is infected with a virus or suffers one or more symptoms of infection from said virus.

11. The method of claim 7, wherein said antigen formulation is non-toxic to said human or said animal.

12. The method of claim 7, wherein said antigen is chose from the HIV antigens: gp160, gag, pol, Nef, Tat, and Rev; the malaria antigens: CS protein and Sporozoite surface protein 2; the Hepatitis B surface antigens: Pre-S1, Pre-S2, HBc Ag, and HBe Ag; the influenza antigens: HA, NP and HA; Hepatitis A surface antigens; Hepatitis C surface antigens; the Herpes virus antigens: EBV gp340, EBV gp85, HSV gB, HSV gD, HSV gH, HSV early protein product, cytomegalovirus gB, cytomegalovirus gH, and IE protein gp72; the respiratory syncytial virus antigens: F protein, G protein, and N protein; and the tumor antigens: carcinoma CEA, carcinoma associated mucin, carcinoma P21, carcinoma P53, melanoma MPG, melanoma p97, MAGE-1, MAGE-3, gp100, MART-1, carcinoma mutated EGF receptor, prostate carcinoma specific antigen (PSA), prostate specific membrane associated antigen, and carcinoma Neu oncogene product, carcinoma mutated EGF receptor, carcinoma p53 gene product, and mutated p21 ras protein.

13. A method of treating a patient infected with HIV virus, comprising administering a composition comprising an HIV antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

14. The method of claim 13, wherein said HIV antigen is selected from gp160, gag, pol, Nef, Tat, and Rev. 77

15. A method of treating a patient suffering from malaria, comprising administering a microfluidized composition comprising a malaria-associated antigen mixed with an antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

16. The method of claim 15, wherein said malaria-associated antigen is selected from CS protein, and Sporozoite surface protein 2.

17. A method of treating a patient suffering from influenza, comprising administering a composition comprising an influenza-associated antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

18. The method of claim 17, wherein said influenza-associated antigen is selected from HA, NP, and NA.

19. A method of treating a patient suffering from hepatitis, comprising administering a composition comprising a hepatitis-associated antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

20. The method of claim 19, wherein said hepatitis-associated antigen is selected from hepatitis A surface antigen, Pre-S1, Pre-S2, HBc Ag, and HBe Ag.

21. A method of treating a patient suffering from a cancer, comprising administering a composition comprising a cancer-associated antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

22. A method of claim 21, wherein said cancer-associated antigen is selected from Carcinoma CEA, Carcinoma associated mucin, P21, carcinoma P53, melanoma MPG, melanoma p97, MAGE-1, MAGE-3, gp100, MART-1, carcinoma mutated EGF receptor, and carcinoma Neu oncogene product, carcinoma p53 gene product, and mutated p21 ras protein.

23. A method of treating a patient infected with herpes virus, comprising administering a composition comprising a herpes antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

24. The method of claim 23, wherein said herpes virus antigen is selected from EBV gp340, EBV gp85, HSV gB, HSV gD, HSV gH, HSV early protein product, cytomegalovirus gB, cytomegalovirus gH and IE protein gP72.

25. A method of treating a patient infected with respiratory syncytial virus, comprising administering a composition comprising a respiratory syncytial antigen mixed with a microfluidized antigen formulation comprising:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation lacking an immunostimulating peptide component, and being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic-T-lymphocyte response in said patient.

26. The method of claim 25 wherein said Respiratory Syncytial virus antigen is selected from F protein, G protein, and N protein.

27. A method for inducing a cytotoxic T-lymphocyte response in a human or domesticated or agricultural animal, comprising the steps of:

administering a mixture of an antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion;

wherein said mixture is administered to said human or animal in an amount sufficient to induce a cytotoxic T-lymphocyte response in said human or animal.

28. The method of claim 27, wherein said human or domesticated or agricultural animal is infected with a virus and suffers one or more symptoms of infection from said virus.

29. The method of claim 27, wherein said antigen formulation is non-toxic to said human or domesticated or agricultural animal.

30. The method of claim 27, wherein said antigen is chosen from antigenic portions of the HIV antigens: gp160, gag, pol, Nef, Tat, and Rev; the malaria antigens: CS protein and Sporozoite surface protein 2; the Hepatitis B surface antigens: Pre-S1, Pre-S2, HBc Ag, and HBe Ag; the influenza antigens: HA, NP and NA; Hepatitis A surface antigens; Hepatitis C surface antigens, the Herpes virus antigens: EBV gp340, EBV gp85, HSV gB, HSV gD, HSV gH, HSV early protein product, cytomegalovirus gB, cytomegalovirus gH, and IE protein gp72; the respiratory syncytial virus antigens: F protein, G protein, and N protein; and the tumor antigens carcinoma CEA, prostate carcinoma specific antigen (PSA), prostate specific membrane associated antigen, carcinoma associated mucin, carcinoma P21, carcinoma P53, melanoma MPG, melanoma p97, MAGE-1, MAGE-3, gp100, MART-1, carcinoma Neu oncogene product, carcinoma mutated EGF receptor, carcinoma p53 gene product, and mutated p21 ras protein.

31. A method of treating a patient infected with HIV virus, comprising administering a composition comprising an HIV antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

32. The method of claim 31, wherein said HIV antigen is selected from gp160, gag, pol, Nef, Tat, and Rv.

33. A method of treating a patient suffering from malaria, comprising administering a composition comprising a malaria-associated antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

34. The method of claim 33, wherein said malaria-associated antigen is selected from CS protein, and Sporozoite surface protein 2.

35. A method of treating a patient suffering from influenza, comprising administering a composition comprising an influenza-associated antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

36. The method of claim 35, wherein said influenza-associated antigen is selected from HA, NP, and NA.

37. A method of treating a patient suffering from hepatitis, comprising administering a composition comprising a hepatitis-associated antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

38. The method of claim 37, wherein said hepatitis-associated antigen is selected from hepatitis A surface antigen, Hepatitis C surface antigen, Pre-S1, Pre-S2, HBc Ag, and HBe Ag.

39. A method of treating a patient suffering from a cancer, comprising administering a composition comprising a cancer-associated antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

40. The method of claim 39, wherein said cancer-associated antigen is selected from Carcinoma CEA, prostate carcinoma specific antigen (PSA) prostate

specific membrane associated antigen, Carcinoma associated mucin, P21, carcinoma P53, melanoma MPG, melanoma p97, MAGE-1, MAGE-3, gp100, MART-1, carcinoma Neu oncogene product, carcinoma mutated EGF receptor, carcinoma p53 gene product, and mutated p21 ras protein.

41. A method of treating a patient infected with herpes virus, comprising administering a composition comprising a herpes antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient.

42. The method of claim 41, wherein said herpes virus antigen is selected from EBV gp340, EBV gp85, HSV gB, HSV gD, HSV gH, HSV early protein product, cytomegalovirus gB, cytomegalovirus gH and IE protein gP72.

43. A method of treating a patient infected with respiratory syncytial virus, comprising administering a respiratory syncytial antigen mixed with a microfluidized antigen formulation consisting essentially of two of:

- (a) a stabilizing detergent,
- (b) a micelle-forming agent, and
- (c) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said composition is administered to said patient in an amount sufficient

to induce a cytotoxic T-lymphocyte response in said patient.

44. The method of claim 43 wherein said Respiratory Syncytial virus antigen is selected from F protein, G protein, and N protein.

45. The method of any of claims 25-44 wherein said antigen formulation consists essentially of said detergent and said micelle-forming agent.

46. The method of any of claims 25-44 wherein said antigen formulation consists essentially of said detergent and said oil.

47. The method of any of claims 25-44 wherein said antigen formulation consists essentially of said oil and said micelle-forming agent.

48. The composition of claim 6 wherein said papillomavirus antigen is selected from the group consisting of the HPV16 E6 antigen, HPV16 E7 antigen, HPV18 E6 antigen, HPV18 E7 antigen, HPV6 E4 antigen, HPV6 L1 antigen, HPV11 E4 antigen and HPV11 L1 antigen.

49. A method for treating cervical cancer comprising administering an effective amount of a human papillomavirus antigen formulation according to claim 48.

50. A method for treating condyloma acuminata comprising administering an effective amount of a papillomavirus antigen formulation according to claim 48.

51. A method for treating prostate cancer comprising administering a composition according to claim 6 wherein the antigen is the prostate specific antigen.

52. The composition of claim 1 wherein the stabilizing detergent is selected from the group consisting of polysorbate 80, Tween 20, Tween 40, Tween 60, Zwittergent 3-12, Teepol HB7 and Span 85.

53. The composition of claim 1 wherein said detergent is provided in an amount ranging from approximately 0.05 to 0.5%.

54. The composition of claim 53 wherein said amount of detergent is about 0.2%.

55. The composition of claim 1 wherein said micelle-forming agent comprises a hydrophile-lipophile balance of between 0 and 2.

56. The composition of claim 1 wherein said micelle-forming agent is selected from the group consisting of poloxamer 401, Pluronic L62LF, Pluronic L101, Pluronic L64, PEG1000, Tetronic 1501, Tetronic 150R1, Tetronic 701, Tetronic 901, Tetronic 1301, and Tetronic 130R1.

57. The composition of claim 1 wherein the amount of said micelle-forming agent ranges from between 0.5 to 10%.

58. The composition of claim 57 wherein the amount of said micelle-forming agent ranges from between 1.25 and 5%.

59. The composition of claim 1 wherein the oil exhibits a melting temperature less than 60°C.

60. The composition of claim 59 wherein the oil is selected from the group consisting of squalene, squalane, eicosane, tetratetracontane, pristane, glycerol, and vegetable oils.

61. The composition of claim 1 wherein the amount of the oil ranges from between 1 and 10%.

62. The composition of claim 61 wherein the amount of the oil ranges from between 2.5 and 5%.

63. The composition of claim 1 which comprises less than 20 micrograms of muramyl dipeptide.

64. The composition of claim 63 does not comprise any muramyl dipeptide.

65. The composition of claim 1 wherein the detergent is polysorbate 80, and the micelle-forming agent is poloxamer 401.

66. The composition of claim 65 wherein the oil is squalane.

67. The composition of claim 1 wherein the detergent is selected from the group consisting of Tween 20, Tween 40 and Tween 80; the oil is selected from the group consisting of squalane, eicosane, and pristane and the micelle-forming agent is selected from the group consisting of Pluronic L62LF and polyoxamer 401.

68. The method of claim 7 wherein the detergent is selected from the group consisting of polysorbate 80,

Tween 20, Tween 40, Tween 60, Zwittergent 3-12, Teepol HB7 and Span 85.

69. The method of claim 7 wherein said detergent is provided in an amount ranging from approximately 0.05 to 0.5%.

70. The method of claim 69 wherein the amount of detergent is about 0.2%.

71. The method of claim 7 wherein said micelle-forming agent comprise a hydrophile-lipophile balance of between 0 and 2.

72. The method of claim 7 wherein said micelle-forming agent is selected from the group consisting polyoxamer 401, Pluronic L62LF, Pluronic L101, Pluronic L64, PEG1000, Tetronic 1501, Tetronic 150R1, Tetronic 701, Tetronic 901, Tetronic 1301 and Tetronic 130R1.

73. The method of claim 7 wherein the amount of said micelle-forming agent ranges from between 0.5 to 10%.

74. The method of claim 71 wherein the amount of said micelle-forming agent ranges from between 1.25 and 5%.

75. The method of claim 7 wherein the oil exhibits a melting temperature of less than 60°C.

76. The method of claim 7 wherein the oil is selected from the group consisting of squalene, eicosane, tetratetracontane, glycerol, pristane, and vegetable oils.

77. The method of claim 7 wherein the amount of oil ranges from between 1 and 10%.

78. The method of claim 77 wherein the amount of oil ranges from between 2.5 and 5%.

79. The method of claim 7 wherein the admixture comprises less than 20 micrograms of muramyl dipeptide.

80. The method of claim 7 wherein the admixture does not contain any muramyl dipeptides.

81. The method of claim 7 wherein the detergent is polysorbate 80 and the micelle-forming agent is poloxamer 401.

82. The method of claim 81 wherein the oil is squalane.

83. The method of claim 7 wherein the detergent is selected from the group consisting of Tween 20, Tween 40 and Tween 80, the oil is selected from the group consisting of squalane, eicosane, olive oil and pristane and the micelle-forming agent is selected from the group consisting of polyoxamer 401, and Pluronic L62LF.

84. The method of claim 7 wherein the particle sizes in the admixture range from 100 to 300 nm.

85. ~~The composition of claim 1 wherein the particle sizes in the composition range from 100 to 300 nm.~~